

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number  
**WO 2004/052389 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 38/17**,  
G01N 33/68, A61P 25/00, 25/08, 9/00

(21) International Application Number:  
PCT/GB2003/005329

(22) International Filing Date: 5 December 2003 (05.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/431,549 6 December 2002 (06.12.2002) US  
60/480,138 20 June 2003 (20.06.2003) US

(71) Applicant (for all designated States except US): **SINGAPORE GENERAL HOSPITAL PTE LTD.** [SG/SG]; 11 Third Hospital Avenue, #07-00, SNEC Building, Singapore 168751 (SG).

(71) Applicant (for MN only): **FORREST, Graham, R.** [GB/GB]; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **XIAO, Zhi-Cheng** [CA/SG]; 173 Chin Swee Road, #32-02, Singapore 169878 (SG).

(74) Agents: **FORREST, Graham, R.** et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
21 October 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **NOGO, CASPR, F3 NB-3 USEFUL IN THE TREATMENT OF INJURY AND DISEASE TO THE CENTRAL NERVOUS SYSTEM**

(57) Abstract: The application provides materials and methods for promoting myelination of neuronal axons in the CNS. These derive from the findings firstly that the molecules Nogo and Caspr interact with one another during establishment and maintenance of the axoglial junction, and secondly that the molecules F3 and NB-3 are capable of promoting oligodendrocyte maturation via interaction with Notch. The materials and methods provided may be used in the treatment of CNS damage, in particular the treatment of spinal cord injury, multiple sclerosis, epilepsy and stroke.

WO 2004/052389 A3

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/05329

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K38/17 G01N33/68 A61P25/00 A61P25/08 A61P9/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 465 210 B1 (PELES ELIOR) 15 October 2002 (2002-10-15) the whole document	1-26
A	----- WO 00/05364 A (SMITHKLINE BEECHAM PLC) 3 February 2000 (2000-02-03) page 1, lines 19-41	1-26
A	----- WO 01/36631 A (SMITHKLINE BEECHAM PLC) 25 May 2001 (2001-05-25) page 1, lines 22-32 ----- -/-	1-26

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

14 April 2004

Date of mailing of the international search report

23.08.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Deck, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05329

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>BHAT M A ET AL: "Axon-glia interactions and the domain organization of myelinated axons requires neurexin IV/Caspr/Paranodin."  NEURON. UNITED STATES MAY 2001, vol. 30, no. 2, May 2001 (2001-05), pages 369-383, XP002276824  ISSN: 0896-6273  cited in the application  the whole document</p>	1-26
A	<p>HAUBEN EHUD ET AL: "Vaccination with a Nogo-A-derived peptide after incomplete spinal-cord injury promotes recovery via a T-cell-mediated neuroprotective response: Comparison with other myelin antigens"  PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 98, no. 26, 18 December 2001 (2001-12-18), pages 15173-15178, XP002244559  ISSN: 0027-8424  the whole document</p>	1-26
T	<p>WOOLF CLIFFORD J: "No Nogo: now where to go?"  NEURON. UNITED STATES 24 APR 2003, vol. 38, no. 2, 24 April 2003 (2003-04-24), pages 153-156, XP009029092  ISSN: 0896-6273  the whole document</p>	1-26
P,X	<p>NIE DU-YU ET AL: "Nogo-A at CNS paranodes is a ligand of Caspr: possible regulation of K(+) channel localization."  THE EMBO JOURNAL. ENGLAND 3 NOV 2003, vol. 22, no. 21, 3 November 2003 (2003-11-03), pages 5666-5678, XP002276825  ISSN: 0261-4189  the whole document</p>	1-26

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/05329

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 16-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-26

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

**Continuation of Box I.1**

Although claims 16-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-26

Composition comprising Nogo and Caspr; use thereof in the treatment of injury or disease of the CNS, for stimulating myelination of a neural axon; screening for modulators of the Nogo-Caspr interaction.

---

2. claims: 27-62

Composition comprising F3 and NB-3; use of F3 and/or NB-3 in the treatment of injury or disease of the CNS, for stimulating differentiation of an oligodendrocyte or myelination of a neural axon; screening for modulators of the Notch-F3 and/or NB-3 interaction.

---

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/05329

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
US 6465210	B1	15-10-2002	WO	9735872 A1	02-10-1997
			US	2003120051 A1	26-06-2003
WO 0005364	A	03-02-2000	EP	1098972 A1	16-05-2001
			WO	0005364 A1	03-02-2000
			JP	2002522016 T	23-07-2002
			US	2002010324 A1	24-01-2002
WO 0136631	A	25-05-2001	EP	1147192 A1	24-10-2001
			WO	0136631 A1	25-05-2001